UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,363	07/18/2003	Steven M. Ruben	PZ013P2C1	8429

22195 7590 07/14/2004

HUMAN GENOME SCIENCES INC
INTELLECTUAL PROPERTY DEPT.
14200 SHADY GROVE ROAD
ROCKVILLE, MD 20850

EXAMINER	
ZEMAN, MARY K	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

SM.

Office Action Summary	Application No.	Applicant(s)	
	10/621,363	RUBEN ET AL.	
	Examiner	Art Unit	
	Mary K Zeman	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 July 2003* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim 1 is pending in this application.

Applicant's election of Group I, claim 1, SEQ ID NO: 12 in the reply filed on 5/5/04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

Applicant's claims to priority to multiple provisional and nonprovisional applications is acknowledged. The earliest disclosure of the sequence of SEQ ID NO: 12 appears to be in PCT US98/16235 filed 8/4/98. The claim is accorded that filing date. Should Applicant desire priority to an earlier provisional application that is not in compliance with the sequence rules, specific reference to the provisional application by page and line number to the sequence should be made in the response.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

35 U.S.C. 101/112 Utility Rejections

The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claim 1 is rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or a well established utility.

The claimed subject matter is not supported by a specific, substantial, and credible utility because the disclosed uses are generally applicable to broad classes of this subject matter. In addition, further characterization of the claimed subject matter would be required to identify or reasonably confirm a "real world" use. The examiner does not find an adequate nexus between the evidence of record and the asserted properties of the claimed subject matter.

The specification identifies SEQ ID NO: 12, the elected polynucleotide sequence, as being related to "gene 2" at pages 9-10. SEQ ID NO: 12 is also referenced in the table at page 69. At pages 9-10, the specification asserts that the polypeptide sequence encoded by "gene 2" shares unspecified sequence homology with ApoE4L1. Neither the level of homology or placement of homology within the sequence are disclosed. It is not clear whether the homology is at the level of the polynucleotide or the polypeptide. The specification asserts that the ApoE4L1 protein is "thought to be important in catalyzing the formation of abnormal beta/A4 variants of beta amyloid protein." This is not an assertion of a specific activity. What exactly this ApoE4L1 sequence does in the "formation" process is not set forth, nor does it appear to be well established in the art. No specific utility for SEQ ID NO:12 is disclosed, and the ApoE4l1 polypeptide does not appear to have a well established utility. Therefore, there is no well established utility for the elected sequence.

At pages 9-10 the specification list a variety of potential activities and tissue "specificities" that *may* be related to the elected polynucleotides, or where the elected sequences may have a use. Activities and specificities for the DNA and/or encoded protein listed in this section include: expression in kidney medulla. Diseases listed include: renal disease, urogenital disease, metabolic disorders, renal failure, nephritus, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic, kidney stones, Wilm's Tumor, congenital kidney abnormalities, Tay-Sach's disease, phenyketonuria, galactosemia, hyperlipidemia, porphyria and Hurler's syndrome. No data is present indicating that the expression of the elected peptide is diagnostic for a type of tissue or disease state. At no point is the specifically elected sequence tested for any of the listed activities or expression patterns. At no point is a diagnostic test for any disease developed such that the elected sequence is shown to be linked diagnostically to a particular disease. Each of the above activities is very different, and they are substantially non-overlapping. Each of these categories of disease have widely varying etiology, causes, and treatments, and the specification provides no particular evidence linking the claimed protein to any particular disease, or even class of diseases. One of skill in the art would not readily be able to determine a use for the claimed sequence upon reading the specification.

The specification was further probed for information as to a specific substantial and credible utility for the claimed peptide. At page 196, in the table, SEQ ID NO: 12 is identified as encoding SEQ ID NO: 109. The related deposit number is HKMMV77 (ATCC209179). The table asserts that the polypeptide has a signal sequence beginning with amino acid 1, and ending with amino acid 15, and asserts that the secreted portion would be from amino acids 16-46. This information was all generated by computer analysis and has not been validated by producing the polypeptide in vitro and observing cleavage and secretion of the actual sequence. No such experiments are set forth in the specification as filed. No particular activities or functions are specifically linked to any form of the polypeptides being claimed.

Absent factual evidence, one skilled in the art would have reason to doubt that sequence similarity alone would reasonably support the assertion that the biological activity of the claimed subject matter would be the same as that of any purportedly similar sequence. Note that it would have been well known in the art that sequence similarity does not reliably correlate to structural

similarity and that structural similarity does not reliably result in similar or identical biological activities. For example, it would have been well known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Iyer et al. Genome Biology 2001 2 (12) pages 1-11; and Baker et al. Science, October, 2001, Vol. 294 pages 93-95. (Both of record in the parent application 09/969730) However, this level of factual evidence is absent here.

General uses of polypeptides set forth in the specification, as filed, include treatment or prevention of unidentified diseases, identification of binding partners, use in production of antibodies to the polypeptides, etc. These general uses are not specific and substantial, as they do not require any one particular sequence. Further, they provide no specific information about any one sequence. For example, for the asserted utility of prevention, diagnosis or treatment of a disease, one would need to know what disease is linked to the polypeptide, and in what way- i.e. does the disease result from too much or too little of the claimed polypeptide. Therefore one of ordinary skill in the art would have to perform additional tests to determine which specific disease could be linked, how it could be linked, and whether or not the peptide itself can be used to treat, prevent or diagnose that disease.

The need for such further research and experimentation clearly indicates that the asserted utilities for the polypeptides are not disclosed and therefore are not specific, substantial and credible utilities Further no well established utility is supported for any one polypeptide. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. Identifying and studying the properties of the claimed subject matter itself or the mechanisms in which the claimed subject matter is involved does not define a "real world" context or use. Similarly, the other listed and asserted utilities as summarized above or in the

instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the claimed polypeptides such that another non-asserted utility would be well-established for the compounds.

Applicant should explicitly identify a specific, substantial, and credible utility for the claimed invention and establish a probative relation between any evidence of record and the originally disclosed properties of the claimed invention.

Claim 1 remains also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by a specific, substantial, and credible utility or a well-established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

The above rejected claims recite polypeptides having various levels of similarity or homology to SEQ ID NO: 12 or the related deposit. The specification, as filed, fails to provide written description of the scope of polynucleotides meeting the limitations of the claims. The specification provides SEQ ID NO: 12, the deposited clone number. The claim as written encompasses an innumerable collection of sequences with minimal relationship to SEQ ID NO: 12. The claim is drawn to SEQ ID NO: 12, the complement, anything that hybridizes, fragments, fragments of things that hybridize, polynucleotides that encode a fragment of a peptide encoded

by SEQ ID NO: 12, variants, homologs etc. The claims encompass genomic DNA having introns, exons, promoters, enhancers, and terminators, none of which are disclosed.

Written description of an invention requires "a precise definition, such as by structure, formula, chemical name, or physical properties." *Eli Lilly*, 119 F.3d at 1566, 43 USPQ2d at 1404. The specification does not set forth any of these definitions for other polynucleotides which fall within the scope of the claims. An applicant may also show written description of an invention by combining a partial structure, physical properties, or chemical characteristics with a known or disclosed specific function. However, no specific function or activity had been ascribed to any one elected sequence in the specification, as filed.

The written description requirement for any claim drawn to a genus can be met through sufficient description of a representative number of species within the genus. The broadest claim for each the polynucleotide is a separate genus. The specification, as filed, only discloses the single species of the genus, which is not sufficient to support the assertion that Applicant was in possession of the entire genus being claimed.

Therefore, claims drawn to purified polynucleotides consisting of the sequence set forth in SEQ ID NO: 12, but not the full breadth of the claims, would meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The deposit of biological organisms is considered by the Examiner to be necessary for enablement of the current invention see 37 CFR 1.808(a). Specifically, it is noted that the above rejected claims either recite deposited material in the body of the claim or depend from claims reciting the deposited material. The Examiner acknowledges the deposit of organisms under ATCC accession number 209179 in partial compliance with this requirement. However, the deposits are not in full compliance with 37 CFR 1.803-1.809.

If a deposit is made under terms of the Budapest Treaty, then an affidavit or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty *and* that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, than an affidavit or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, should be submitted stating that the deposit has been made at an acceptable depository *and that* the following criteria have been met:

1) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

2) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

3) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

4) a viability statement in accordance with the provisions of 37 CFR 1.807; and

5) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of claim 1 are unclear. The specification fails to clearly define the metes and bounds of a "variant" of a claimed sequence, and an "allelic variant" of a claimed sequence. At what point is a mutated sequence no longer deemed to be related to SEQ ID NO: 12? How much must they retain in common? A single nucleotide? The metes and bounds of "a species homolog" are not defined such that one of skill in the art would be apprised of the sequences that fall within the scope of the claim. Further, the terms "domain" and "epitope" are

not clearly defined such that one of skill in the art would know how much of the polynucleotide sequence is required to meet the limitation of encoding a domain or an epitope. Similarly, fragment is not well defined in the specification and appears to encompass a single nucleotide.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Genbank AA613893.

Genbank AA613893 (18 February 1998) discloses a polynucleotide sequence having 76 consecutive polynucleotides of SEQ ID NO: 12. This sequence would hybridize to SEQ ID NO: 12, would encode a fragment of the encoded polypeptide, is at least 95% identical to a fragment of SEQ ID NO: 12, encodes a domain encoded by SEQ ID NO: 12, etc. As such this disclosure meets the limitations of the claim.

Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by US 6,399,373 (Bougueleret).

Bougueleret (US 6,399,373 having priority to 6/30/1998) discloses a polynucleotide sequence having 58 consecutive polynucleotides of SEQ ID NO: 12. This sequence would hybridize to SEQ ID NO: 12, would encode a fragment of the encoded polypeptide, is at least 95% identical to a fragment of SEQ ID NO: 12, encodes a domain encoded by SEQ ID NO: 12, etc. As such this disclosure meets the limitations of the claim.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (571) 272 0723

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P Woodward can be reached on (571) 272 0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

MARY K. ZEMAN
PRIMARY EXAMINER
AU1631 1/9/04